A Biomarker-Based Framework for the Prediction of Chronic Pain

Preprint

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INTRODUCTION

Chronic pain is a multifactorial condition presenting significant diagnostic and prognostic challenges. Using data from the UK Biobank (n=19,360 - 493,211), we applied machine learning to multi-dimensional biological and psychosocial data to identify biomarkers for chronic pain and pain-associated medical conditions (e.g., rheumatoid arthritis, fibromyalgia, stroke, and gout).

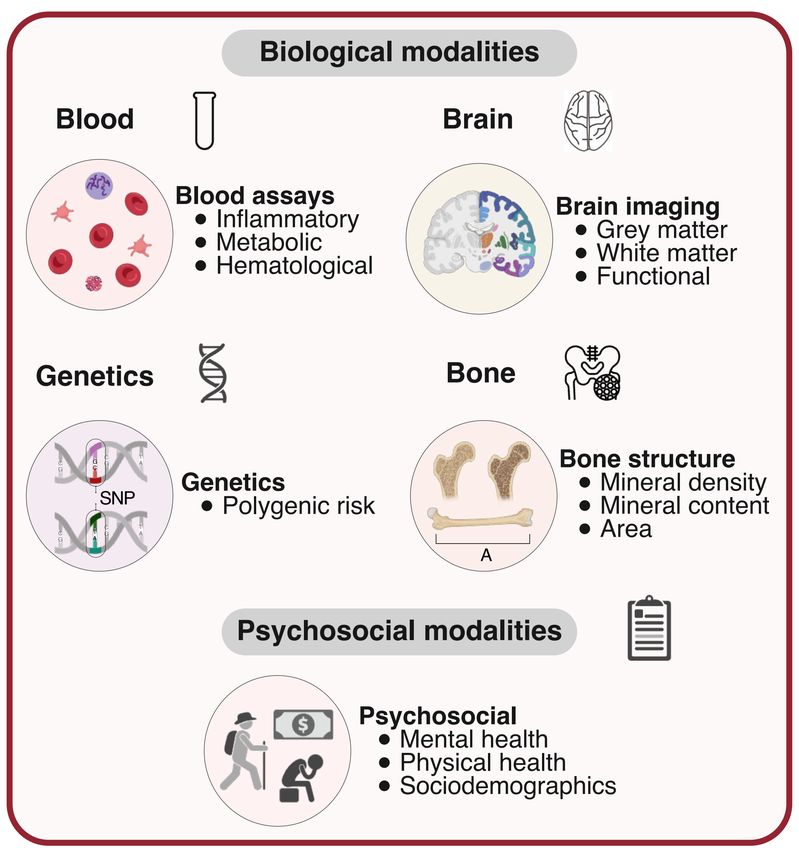
METHODS

Data:

A total of 493,211 individuals were obtained from the UK Biobank (UKBB). 35 pain associated diagnoses were sourced from participants health records Biological modalities indexing four diverse domains of physiological health were selected for analyses including blood immunoassays, polygenic risk scores, bone structure estimates derived from Dual-energy X-ray absorptiometry (DXA) scans, and measures of brain structure and function from brain imaging. Psychosocial data were derived from questionnaires indexing mental, physical, and sociodemographic domains of health.

Analyses:

Logistic regression machine learning algorithms were applied to biological and psychosocial data to classify individuals diagnosed with a pain-associated medical condition from diagnosis-free controls. Biological and psychosocial risk scores were extracted for the best predicted diagnoses based on blood assays and assessed for psychosocial interaction effects associated with longitudinal incidence of diagnoses over 15 years.



Biological and psychosocial modalities used to predict pain-associated medical conditions.

CONCLUSION

Our results provide insight into the potential for diagnostic and prognostic biomarkers across various painful medical conditions. Morover, they imply that painful medical conditions can be accurately predicted through the synergy between biological and psychosocial factors, underscoring the need for a holistic approach in the development of biomarkers to enhance their clinical utility.

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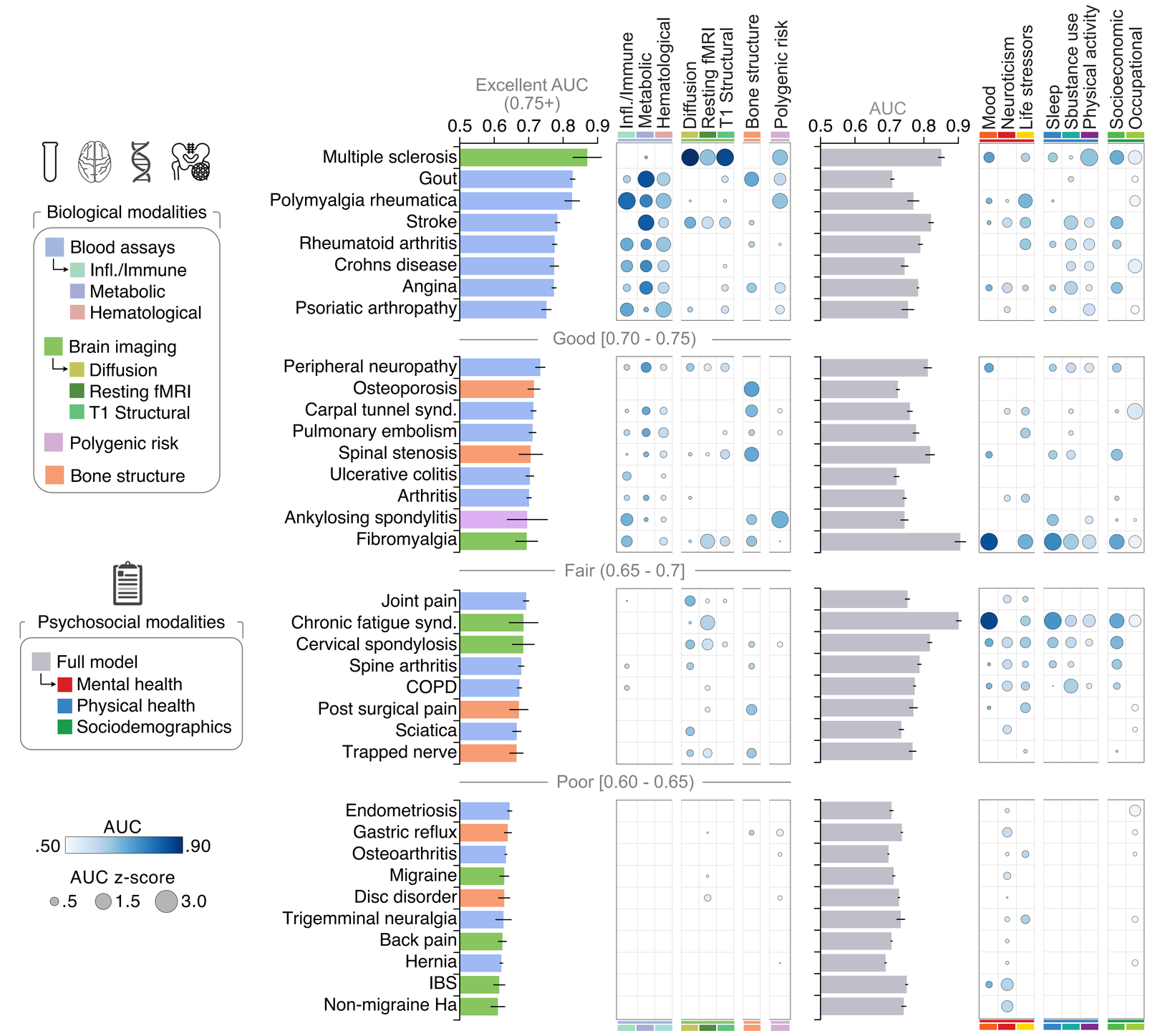
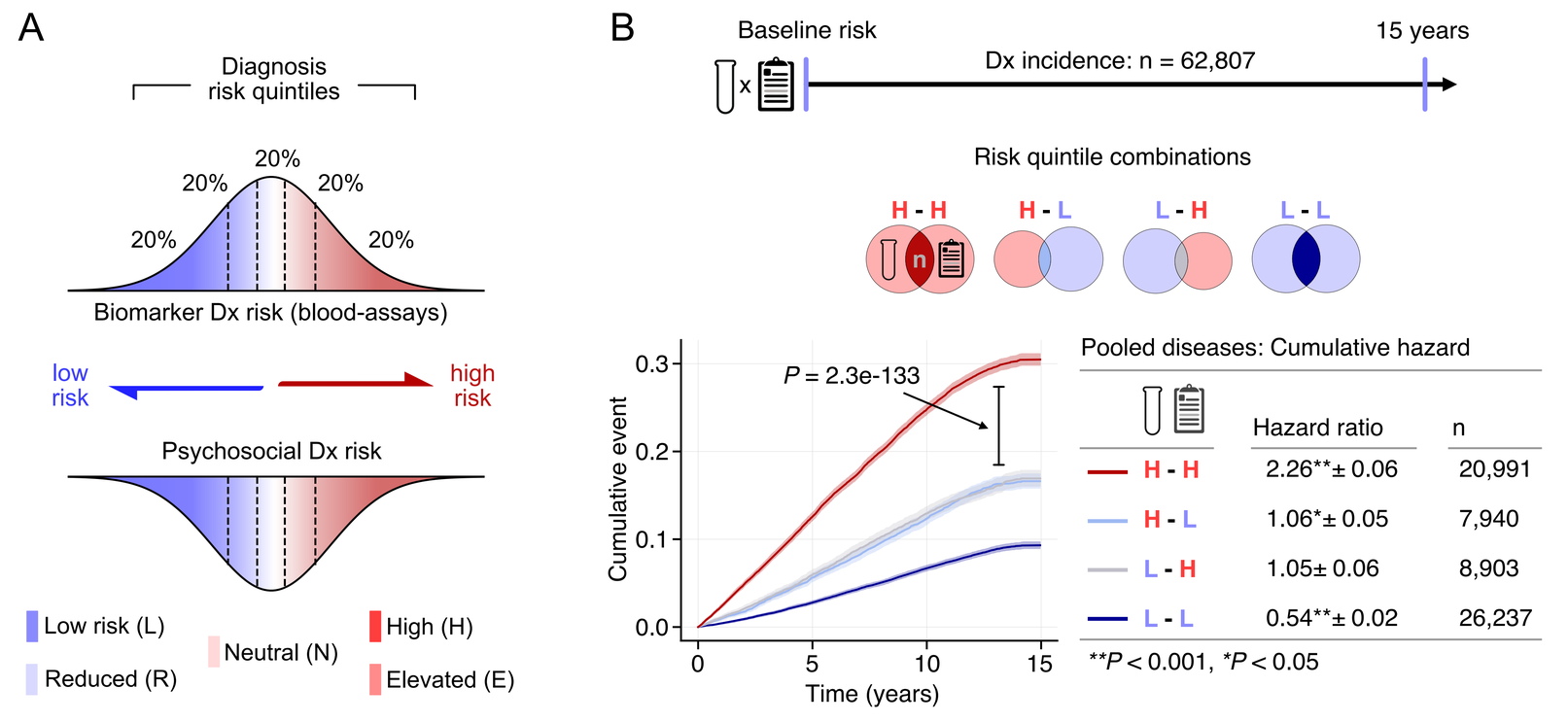
RESULTS

Fig. 1: Classifying pain associated diagnoses using biological and psychosocial modalities



Logistic regression models were used to classify pain associated diagnoses from diagnosis-free controls. The bar charts display the highest ROC-AUC scores for biological (left) and psychosocial (right) modalities for each diagnosis. Accompanying bubble heatmaps illustrate ROC-AUC scores for subcategories, with bubble color and size indicating the absolute AUC score and its z-score compared to other diagnoses. Collectively, these results highlight the complex interplay of biological and psychosocial factors in predicting various pain-related medical diagnoses.

Fig. 2: Assessing biopsychosocial synergy in the prognosis of pain-associated diagnoses



A, Diagnosis risk scores were calculated for the top 12 diagnoses predicted by blood assays by averaging predicted probabilities from blood- and psychosocial-based models. Blood and psychosocial risk scores were categorized into quintiles to indicate biological or psychosocial risk levels for each individual. **B.** Kaplan-Meier curves illustrate the cumulative incidence of diagnoses over 15 years post-baseline, divided into four groups based on combinations of blood-psychosocial risk quintiles (High-High, High-Low, Low-High, Low-Low). Over 15 years, individuals with high risk in both biological and psychosocial factors experienced twice the cumulative incidence of pain-associated diagnoses (HR: 2.26) compared to those with high biomarker but low psychosocial risk (HR: 1.06).